A Novel Fontanelle Probe for Sensing Oxygen Saturation in the Neonate

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Abstract. Continuous monitoring of blood oxygen saturation (SpO_2) of the neonate is essential to the quality of health care provided on a neonatal intensive care unit (NICU). Current saturation sensors are usually placed at the hand or foot, which are dependent of a peripheral blood supply. When the peripheral blood circulation of neonates is compromised conventional peripheral pulse oximeters, in many cases, fail to operate accurately or operate at all. A new reflectance anterior fontanelle (ANTF) SpO_2 sensor and instrumentation has been developed to investigate SpO_2s from the neonatal fontanelle. The underlying hypothesis is that perfusion at such a central site such as the fontanelle should be preferentially preserved at time of compromised peripheral circulation.

Fifteen neonates on an NICU (9 male, 6 female) with a median age of 7 days (IQR = 41.5 days) were selected for ANTF SpO_2 monitoring. ANTF photoplethysmographic (PPG) signals were monitored for a maximum period of two hours, during which delivered oxygen concentration (FiO_2) was artificially altered in order to study the sensitivity of the new custom made sensor compared to a commercial pulse oximeter. The developed system and custom made sensors were successful at acquiring good quality signals at both wavelengths necessary for pulse oximetry calculations. SpO_2 changes at times of FiO_2 change are observable in all three SpO_2 sensors used, confirming the sensitivity of the ANTF sensor. ANTF SpO_2s, estimated from the acquired PPGs, were in broad agreement with SpO_2s obtained from the commercial foot pulse oximeter. A Bland and Altman analysis of the differences between SpO_2s from the fontanelle PPG sensor and the commercial device show a relatively small mean difference ($d = \pm 2.2\%$), but with a wide variation ($2s = \pm 17.4\%$) this observation, however may be due to the varied levels of ill health patients and is backed up by comparing the commercial device SpO_2 readings at the same moment a blood gas sample was taken ($d = -4.8\%, 2s = \pm 15.8\%$).

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1. Introduction

The pulse oximeter relies on the presence of peripheral arterial pulsations, also known as the photoplethysmograph (PPG), which is detected by an optoelectronic sensor comprising an infra red and red light source and a photo-detector. Instrumentation is used to convert the current from the photodiode into voltage signals which are then digitised and used to estimate SpO_2 (Kyriacou et al. n.d.).

It has been shown that various physiological and pathological conditions can cause commercial pulse oximetry sensors to fail in estimating accurately or estimate at all SpO_2 values (Lawson et al. 1987, Morris et al. 1989, Severinghaus & Spellman 1990, Trivedi et al. 1997). In these reviews the ability of the devices under investigation to detect an arterial pulse varied, and even went as far as to point out that some oximeters were in fact very good at detecting pulses of small amplitude (Lawson et al. 1987) when the arm was occluded up to 93% of systolic pressure. Most, if not all, of the studies were performed on adults receiving hospital care or on volunteers.

There is, however, limited knowledge on the performance of pulse oximeters in paediatric or neonatal populations. There have been some studies (Iyer et al. 1996, Levene & McKenzie 1988, Moller et al. 1993, Morgan & Durbin 1986, Reich et al. 1996) where the investigators explored the accuracy of pulse oximeters in paediatric or neonatal populations. The vast majority of PPG/SpO_2 sensors used in these studies were placed on the finger, ear or foot. In conclusion these studies showed that when the patient's peripheral perfusion was poor due to various physiological and/or pathological conditions the accuracy and reliability of the pulse oximeters was compromised. It is ironic that it is at these times that a reliable and almost instantaneous estimation of SpO_2 would be of most benefit to health-care professionals and patients.

Specifically, Villanueva *et al* (Villanueva et al. 1999) set out to assess a selection of pulse oximetry failure criteria in 19 children of 10 years of age or less including blood flow and pulse pressure. The main results concluded that low blood flow, induced artificially by increasing cuff pressure has little effect on the ability of the pulse oximeter to perform its functions, as arterial pulsations at the periphery were still detectable at high occluding pressures. The end of this study noted that it took at least two factors to affect the pulse oximeter significantly, particularly the combination of low skin temperature and low haemoglobin concentration, thus giving support that systemic vasoconstriction, induced by cold periods or hypovolaemia does significantly affect pulse oximeter function.

There is the suggestion (Sedaghat-Yazdi et al. 2008) that some transmission pulse oximetry sensors are less accurate when placed on the sole or palm, as opposed to the finger or toe when SpO_2 is less than 90%. In neonatal and paediatric populations the small dimensions of the infant toe or finger make them inadequate for proper attachment and so accuracy and precision may be also affected when the sensors designed for specific areas of anatomy are alternatively placed.

A number of researchers and manufacturers tried to overcome these problems

by designing various reflectance mode sensors for use in locations where it has been suggested that perfusion is preserved at times when the periphery has failed. These include oesophageal sensors (Kyriacou 2006, Kyriacou et al. 2008, Grubb et al. 2014), and head/scalp/trunk sensors (Faisst et al. 1995, Dassel et al. 1997, Faisst et al. 1997, Berkenbosch & Tobias 2006).

Excellent progress has been made in utilising reflectance PPG technology in neonates as a heart rate monitor (Grubb et al. 2014), and the forehead is acknowledged to better maintain perfusion compared to the extremities. As the vasculature in the forehead is shared almost globally over the entire head it is our belief that other locations could be utilised for PPG monitoring. Grubb *et al* (Grubb et al. 2014) used a one wavelength, green light (525 nm), in their study rather than the traditional two wavelengths of red and infrared light (660 and 940 nm respectively) used for SpO_2 monitoring, citing that this wavelength has better amplitude characteristics that make it ideal for pulsatile/heart rate analysis.

A pilot study on ten adult volunteers (Mendelson et al. 2006) demonstrated that it was possible to acquire SpO_2 readings from the forehead using a reflectance sensor. The sensor was set-up against a conventional finger sensor, where only a small difference in the mean and standard deviation of the values between sites was observed. Other studies into pulse oximetry from the head, whether from paediatrics or adults, showed that they were prone to giving falsely high or low readings when compared against readings from a peripheral location. Six adults and seven neonates were selected for a study (Nijland et al. 1995) to compare the effect of pulsating arteries on reflectance pulse oximetry. To make the comparison the sensor was placed either on the forehead or the temple, where the effect of the superficial temporal artery on pulse oximetry could be studied closely and without any invasive intervention. The orientation of the sensor on the temple was varied between having either the LEDs or the photodiode directly over the blood vessel. When the photodiode was placed over the artery SpO_2s were shown to be lower in both populations (7.5% and 5.8% for neonates and adults respectively) than the reading from the forehead. When the sensor was reorientated, so that the LEDs were over the artery, there was an insignificant change in SpO_2, however the plethysmograph signals were larger than those acquired at the forehead.

It is either the forehead or the temple that seem to be the main focus for reflectance pulse oximetry on the head; this is probably suggestive of the fact that these two locations are generally easy to locate a sensor since there is no obstruction that may be caused by hair. In neonates, who are often born with little or no hair, there exists the opportunity to position the sensor in other scalp locations where SpO_2 monitoring may be unaffected by the phenomena previously described. Two studies of reflectance pulse oximetry in neonates describe at least one other location (Faisst et al. 1995, Dassel et al. 1997).

The first study (Faisst et al. 1995) recruited thirty-one neonates from an ICU who had a reflectance sensor placed on the forehead, cheek, occiput (back of the head) and back, in turn, to determine optimal positioning of the sensor. The second study

(Dassel et al. 1997) solely concentrated on placing the sensor on the scalp (eight separate locations) of only seven healthy infants. In the first study (Faisst et al. 1995) the authors reported close agreements between SpO_2 and heart rate for the reflectance sensor versus a transmission sensor placed simultaneously on the hand. It was noted that the reflectance sensor placed on the lower back was unreliable and susceptible to breathing artefacts. From the plethysmograph signals recorded in the second study (Dassel et al. 1997) it was observed that there was a clear difference in the effect of location, with up to a 13% difference in SpO_2s. Dassel (Dassel et al. 1997) states that the differences observed can be explained by the optical differences of varying tissues at each of the locations. Interestingly it is when there is a space in the skull (over the fontanelle) where the largest red/infra red values are observed, which again can be attributed by specific optical properties of the underlying tissues, and in this case the specific lack of skull.

The chance to study PPGs from the fontanelle and underlying soft tissue was the primary motivation to design and fabricate a reflectance-based sensor that can be located on the anterior fontanelle (ANTF) (May et al. 2011).

The fontanelle are the soft areas of unformed skull on a new born that aid in the birthing procedure, distorting the shape of the head temporarily for easier passage through the birth canal. They also aid in the rapid growth of the head during infancy, and dont fully solidify until about 24 months old (Graaff et al. 2009).

The motivation of this study is to investigate for the first time PPGs and SpO_2s acquired from the ANTF and to compare them with PPGs and SpO_2S acquired from a peripheral site such as the foot. The hypothesis underlying this study is that the perfusion of the brain will be preferentially preserved at times where the periphery is compromised and hence peripheral pulse oximeters might fail to estimate accurately blood oxygen saturation, while the ANTF pulse oximeter will provide reliable monitoring of SpO_2.

2. Materials and Methods

2.1. Instrumentation

Optically and electrically identical reflectance ANTF and foot PPG sensors and instrumentation have been designed and developed. The technical details of these developments have been reported in the literature (May et al. 2011).

In brief an ANTF and foot reflectance PPG sensors were constructed using a flexible PCB substrate (Pyralux, DuPont, USA). The red (660 nm) and infrared (940 nm) LEDs were of identical dimensions (2 1.25 1.1 mm, LxWxH) (KP-2012 series, Kingbright, Taiwan) and were arranged in a dual-light source configuration 5 mm either side of the photo-diode (5 4.25 1.12 mm, LxWxH, active area = 7.5 mm^2) (TEMD5010X01, Vishay, USA) figure 1.

The ANTF sensor was enclosed within a medical-grade clear epoxy resin, to isolate

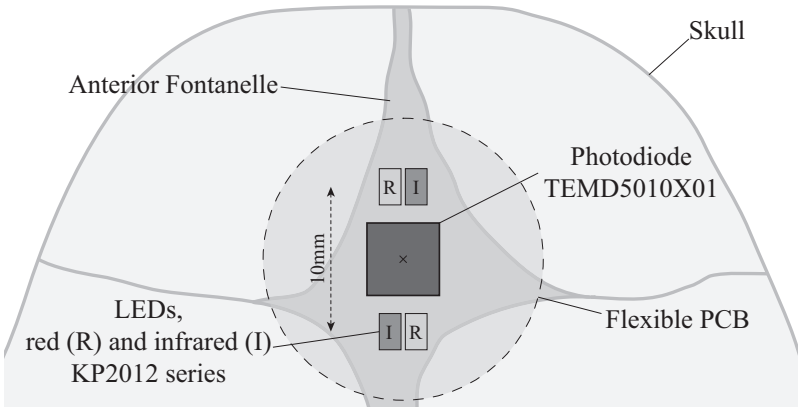

Figure 1. Top-down oblique view of neonatal skull and anterior fontanelle, with the concept of sensor component layout overlaid.

it electrically, and placed within a de-constructed ECG patch. It was terminated with a flat ribbon cable and connector.

A PPG processing system was also designed and fabricated to; drive and multiplex the LEDs (red and near infra red); convert the returning photo-diode current to a voltage signal; de-multiplex the voltage PPG signal into separate signals for the red and infra red LEDs; and filter any unwanted noise. A data-acquisition card (DAQ) (16-bit, USB-6212, National Instruments, USA) was used to digitise (Fs = 200 Hz) the raw PPG signals. The electronics and DAQ were enclosed, with dedicated DC power supply (two parallel 12 V, 2 Ah batteries), into an electronically shielded instrumentation case with external connectors for the separate PPG sensors, USB data cable and controls for adjusting the LED drive current and gain of the transimpedance amplifier.

A custom LabVIEW (National Instruments, USA) data-acquisition virtual instrument (VI) was developed for interfacing with the DAQ card, and for displaying the PPG signals in real time and performed online heart rate and SpO_2 estimation. The VI stored the unprocessed signals for further off-line analysis.

2.2. Clinical Measurements

Following research ethics approval and parental consent, measurements were carried out on 15, ASA I, II and III (American Society of Anaesthesiologists physical status classification system) neonates (9 male, 6 female) with a median gestational age of 7 days (inter-quartile range = 41.5 days) and a median weight of 3.2 kg (SD = 0.8 kg). The study took place in the neonatal intensive care unit of Great Ormond Street Hospital for Children, London, UK.

Candidates were selected on ward rounds by the lead clinician against the list of inclusion/exclusion criteria specified in the approved protocol. Candidates were excluded from the study if they were born at less than 36 weeks gestation, had abnormal fontanelle anatomy, were not sedated and not receiving any complimentary respiratory or oxygen support.

Five ASA I patients (not on mechanical respiratory support, but receiving complimentary oxygen therapy) seven ASA II patients (on conventional ventilator respiratory support), and 3 ASA III patients (on oscillator breathing support) were recruited for this study. Prior to the study the ANTF and foot sensors were cleaned with alcohol wipes and placed into clear adhesive sterile pockets (TegadermTM, 3M, USA). The custom made foot PPG sensor was secured on the sole of the foot with standard medical tape. A commercial transmission SpO_2 sensor (Phillips Medical, USA) was placed on the other foot of the neonate as part of the standard hospital protocol. This commercial pulse oximetry sensor enabled comparative SpO_2 studies with the custom made ANTF sensor.

The lead clinician manoeuvred the ANTF sensor over the fontanelle until PPGs with good quality were observed. The ANTF sensor was then secured into position with a bandage that was wrapped around the back of the head. Figure 2 shows the experimental set up of the ANTF PPG monitoring with the foot PPGs as a reference.

At the time of the next routine blood sample for blood gas analysis, the study was commenced and time stamped in the data file with a time-stamp function built into the VI. The results from this blood gas analysis were used as the gold-standard, enabling the comparison between the custom made sensors and that of the commercial SpO_2 device.

Monitoring continued for a maximum of thirty minutes in order to establish a baseline PPG reading, after which the fractional inspired oxygen (FiO_2) being

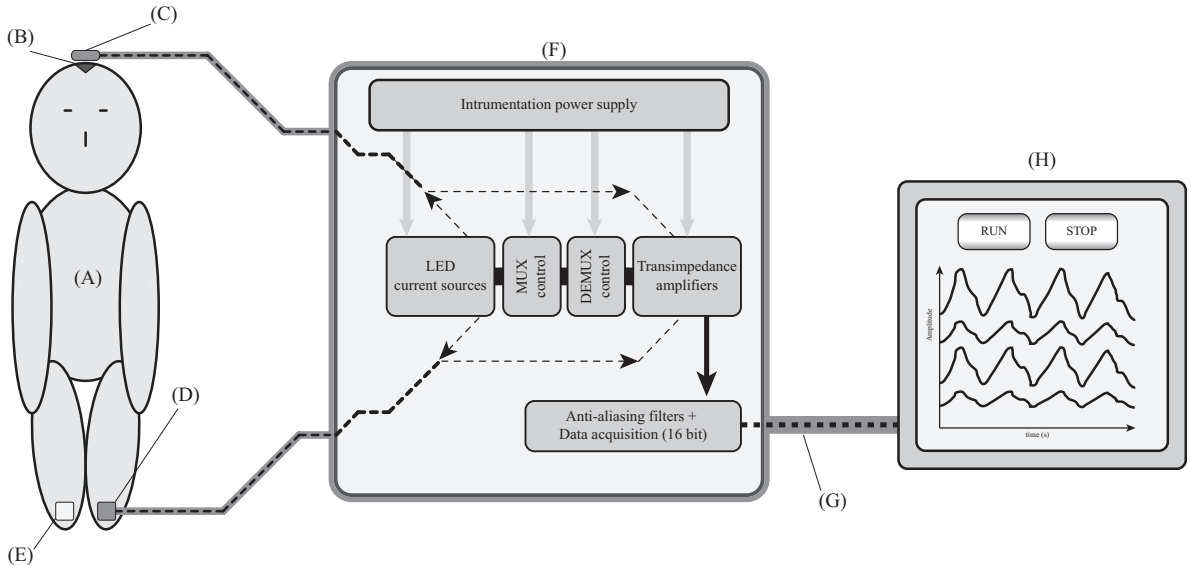

Figure 2. Experimental setup for anterior fontanelle monitoring. The neonate (A) has PPGs simultaneously recorded from the anterior fontanelle (B), using the custom made ANTF sensor (C), and the foot (D). The commercial SpO_2 sensor (E) is left *in situ* for comparative analysis. The custom sensors are connected to the custom instrumentation (F), which is connected via a USB cable (G) to a laptop with custom recording software (H).

administered to the patient as part of the routine care was increased by 50% of the baseline setting and continued for a maximum of one hour, after which FiO_2 was decreased back to the baseline setting. This was done to see if the custom sensor was sensitive to oxygen concentration change. During the study SpO_2 values, heart and respiration rates acquired by commercial medical devices were manually recorded. All blood gas tests carried out during this time were also marked into the raw data file using the time stamp function on the VI.

2.3. Data Analysis

Prior to SpO_2 estimation,the raw PPG signals were inspected analysed with a fast Fourier transform function (FFT), implemented in MATLAB (MathWorks, USA) to determine the most suitable parameters for filtering and signal normalisation. All the PPG signals were normalised using the formula in (1).

$$PPG_N = \frac{PPG_{AC}}{PPG_{DC}} \tag{1}$$

where PPG_{AC} was the AC portion of the signal and PPG_{DC} was the DC portion (**?**).

The normalised signals were filtered using band pass filters implemented in MATLAB (MathWorks, USA). The band-stop and band-pass values were set to incorporate the fundamental frequency due to heart rate for each patient individually, thus eliminating any respiratory (natural or mechanical) artefact.

Time stamps recorded by the user on the VI during the clinical trials, indicating when a blood gas measurement was made, were used to isolate the section of PPG signals at those times. No calibration was made to derive an SpO_2 curve for the custom sensors and system, as the protocol was designed to look for changes in concentration, regardless of the actual SpO_2 value. Instead SpO_2 was estimated using the linear formulae (2) and (3).

$$SpO_2 = 110 - 25R \tag{2}$$

$$R = \frac{PPG_{Nred}}{PPG_{Nir}} \tag{3}$$

described in (Webster 1997) where PPG_{Nred} and PPG_{Nir} were the normalised amplitudes of the red and infrared PPG signals respectively.

The limits of agreement between the ANTF SpO_2 results and those from the commercial toe pulse oximeter and the blood gas analyser were calculated using the between-method differences analysis outlined by Bland and Altman (Bland & Altman 1986).

3. Results

Photoplethysmographs at both wavelengths (red and infrared) were acquired successfully from the fontanelle and the foot of all neonates. Figure 3 shows typical fontanelle and

foot PPGs respectively for the infrared and red wavelengths with respiration modulation.

A comparison of the SpO_2 values obtained from the ANTF vs the commercial device and the gold standard can be seen in the boxplot in figure 4.

A total of 26 pairs of SpO_2 values from the 16 patients were used to compare the ANTF and the commercial foot pulse oximeter. Figure 5 is a plot of the difference between the ANTF and the commercial foot SpO_2 values against their mean. Calculations of the bias, estimated by the mean difference and the standard deviation of the differences were performed to assess the degree of agreement between the two methods. The bias (d) is the ANTF pulse oximeter reading minus the commercial foot pulse oximeter reading and was 2.2% with a standard deviation (s) of $\pm 8.7\%$. Hence, the limits of agreement for the SpO_2 data (ANTF and commercial foot) were:

$$d - 2s = +2.2 - (2 \times 8.7) = -15.2\% \tag{4}$$

$$d - 2s = +2.2 + (2 \times 8.7) = +19.6\% \tag{5}$$

The results from the Bland and Altman analysis of the commercial and fontanelle pulse oximeters showed wide limits of agreement which is uncharacteristic of most pulse

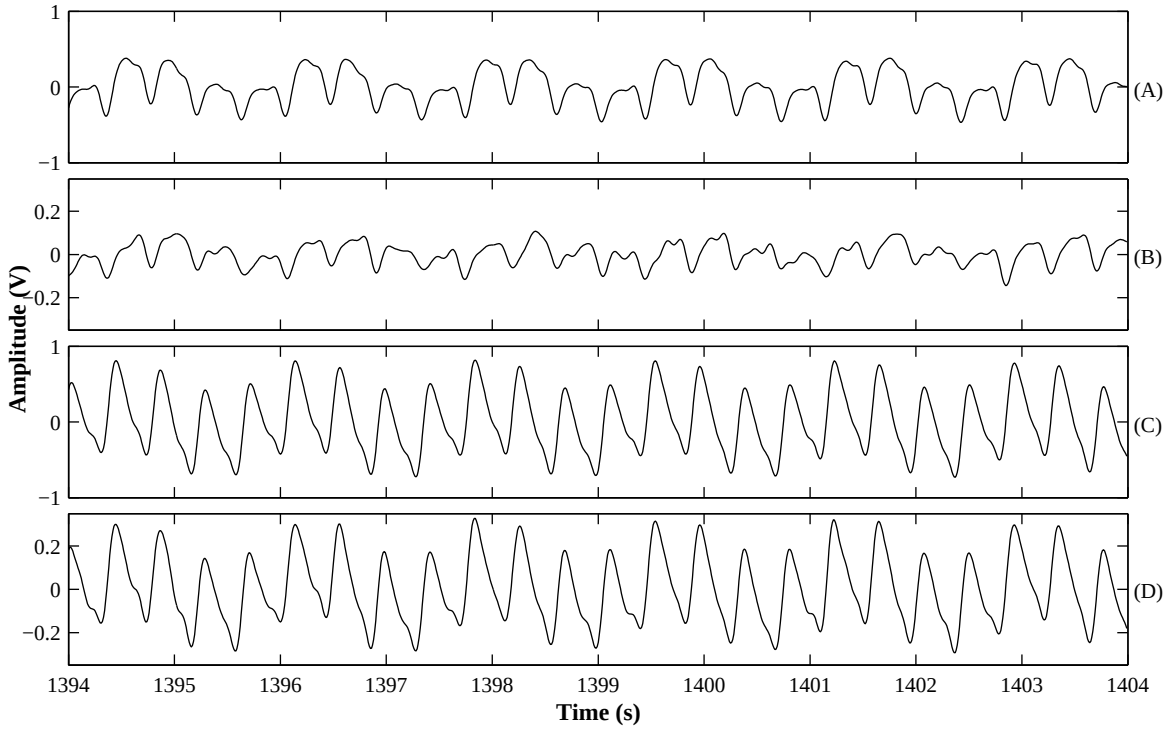

Figure 3. A ten-second sample of PPGs acquired simultaneously from the anterior fontanelle and foot. The infrared and red PPG signals from the ANTF are shown by (A) and (B) respectively, whilst the infrared and red signals acquired from the foot are shown in plots (C) and (D) respectively. Clearly visible are the pulsations due to the heart, and the modulation from breathing. HR ≈ 141 *bpm*, RR ≈ 35.

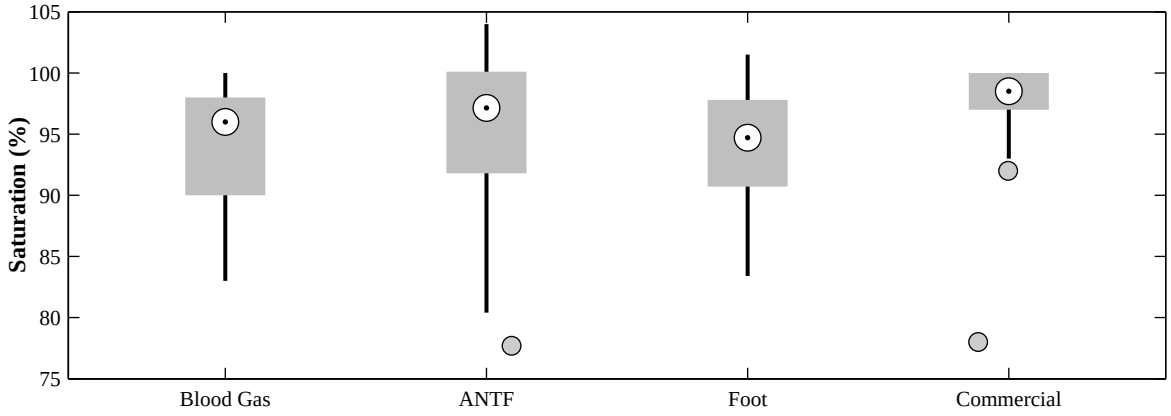

Figure 4. Boxplot of SpO_2(ANTF, foot and commercial device) and Blood Gas (SaO_2) results, n = 26.

oximeters operating within normal conditions.

One of the factors that might have caused such large deviation from the mean is the fact the the custom ANTF pulse oximeter is not calibrated.

In order to investigate this further and establish the source of such deviation another Bland and Altman analysis was performed comparing the gold standard blood gas analysis (BGA) with the commercial foot pulse oximeter. For this analysis a total of 26 pairs of SpO_2 values from the 16 patients were used to compare the commercial foot pulse oximeter with the BGA. Figure 6 is a plot of the difference between the BGA and the commercial foot SpO_2 values against their mean.

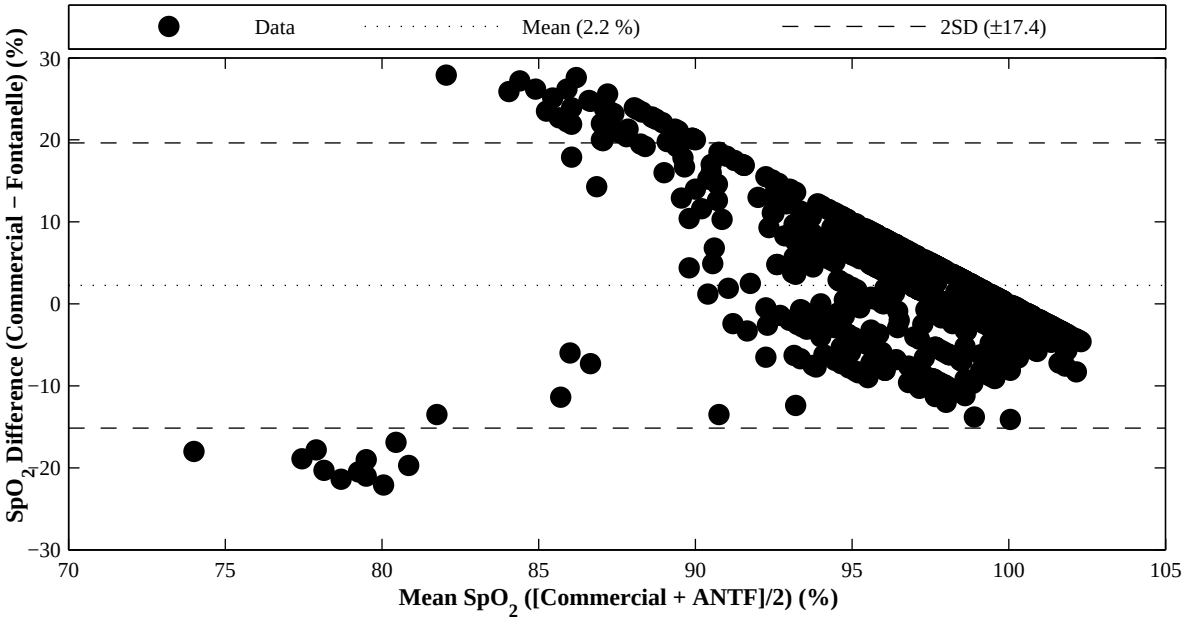

Figure 5. Bland and Altman plot of all SpO2 results (Commercial vs ANTF) from all 15 patients, n = 621.

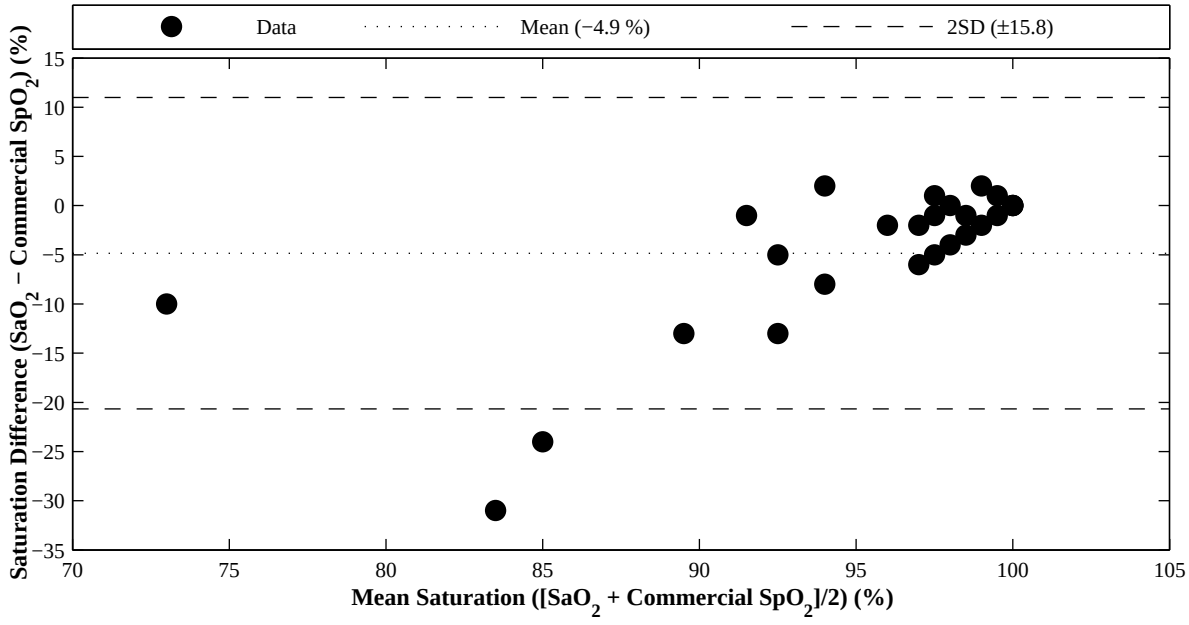

Figure 6. Bland and Altman plot of the saturation results (gold standard SaO_2 vs. commercial) from all 15 patients, n = 26.

The same calculations as described for the ANTF vs the commercial foot SpO_2 were carried out for the BGA verses the foot SpO_2, where a bias (d) of -4.85% and standard deviation (s) of $\pm 7.9\%$ were computed. The limits of agreement for the BGA against Foot SpO_2 were therefore:

$$d - 2s = -4.85 - (2 \times 7.9) = -20.65\% \tag{6}$$

$$d - 2s = -4.85 + (2 \times 7.9) = +10.95\% \tag{7}$$

4. Discussion

This pilot study has shown successfully that PPGs of good quality at both red and infrared wavelengths can be acquired from the neonatal anterior fontanelle.

In figure 4 the boxplot shows the results of SpO_2 estimation at the same moments blood gas samples were taken. In general it can be said that the commercial device and the fontanelle sensor both slightly over-estimate oxygen saturation, but the fontanelle sensor has similar variation to the blood gas results. The wider variation in SpO_2 values compared to the custom foot sensor may be due to the unique anatomy of the fontanelle or localised saturation variations, but this remains a conjecture and needs more rigorous investigation and comparison against another method, such as near infrared spectroscopy (NIRS).

These differences compared to the commercial device may also be due to proprietary on-board processing algorithms that eliminate erroneous SpO_2 values based

on automatic real-time signal analysis, whereas the gold-standard and custom sensors, calculate an instantaneous reading based on the sample taken at that moment using well established numerical methods.

An overall look at the SpO_2 estimation from the fontanelle compared to the commercial device (Phillips Medical pulse oximeter, USA) in the first Bland-Altman analysis, figure 5, reveals only a small difference in SpO_2 estimation (+2.2%), however the large limits of agreement seen in this result ($2s = \pm 17.4\%$) are likely due to the wide variety of observed gold-standard blood gas results (due to varying health of ICU patients), and is backed up by the second Bland-Altman analysis, figure 6, comparing the gold standard with the commercial device ($d = -4.85\%$, $2s = \pm 15.8\%$).

5. Conclusion

The large limits of agreement for the two commercial methods of oxygen saturation measurement (Foot SpO_2 and BGA) would appear to back up the large limits of agreement seen between the fontanelle sensor and the commercial pulse oximeter for this group of patients. A controlled experiment with healthy subjects with similar health may prove useful to help back up this observation further.

From this study it is reasonable to conclude that the fontanelle sensor is at least as accurate as the commercial sensor, even when no specific calibration curve has been determined for this unique anatomical geometry.

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